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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/821,545	04/09/2004	Michael E. Hepperle	MPI03-043P1RNRCEM	1299

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MILLENNIUM PHARMACEUTICALS, INC.
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EXAMINER	
BIANCHI, KRISTIN A	

ART UNIT	PAPER NUMBER
1626	

MAIL DATE	DELIVERY MODE
06/19/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/821,545	HEPPERLE ET AL.	
	Examiner	Art Unit	
	KRISTIN BIANCHI	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03/02/2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,9,17,28 and 29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *28 and 29* is/are allowed.

6)☒ Claim(s) *1,9 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 9, 17, 28, and 29 are pending in the instant application. Claims 28 and 29 appear to be allowable. Claims 1, 9 and 17 are rejected.

Response to Amendment and Arguments/Remarks

Applicants' amendment and arguments/remarks filed on March 2, 2009 have been fully considered and entered into the application. While applicants have stated that the provisional nonstatutory obviousness-type double patenting rejection of claims 1, 9 and 17 will be addressed when allowable subject matter is indicated, the provisional rejection is still considered proper and is, therefore, maintained. The provisional nonstatutory obviousness-type double patenting rejection is altered slightly due to the claim amendments filed (i.e., on May 19, 2008) in the copending application. The 35 USC 103(a) rejection of claims 1, 9 and 17 is also maintained.

In regards to the 35 USC 103(a) rejection of claims 1, 9 and 17, Applicants argue that there is no suggestion or motivation in Castro *et al.*, alone or combined with knowledge generally available in the art, to modify the reference to arrive at the claimed invention, nor does it provide any reasonable expectation that modification of the morpholine ring to include methyl would successfully yield compounds having activity against IKK that would be useful for the disease or disorders described by the Applicants. Applicants also argue that a *prima facie* case of obviousness also requires a showing of adequate support in the prior art for the change in structure. As stated in the Office Action dated August 29, 2008, these arguments are not persuasive because the motivation to make the claimed compounds derives from the expectation, which is

known in the art and was at the time of the invention, that structurally similar compounds possess similar properties and, therefore, similar activities (i.e., the compounds disclosed in Castro *et al.* are used for the same purpose or have the same activity as the compounds disclosed in the instant application, as inhibitors of IKK). Also, to those skilled in the chemical art, one homologue is not an advance over an adjacent member of a homologous series. Therefore, one of ordinary skill, knowing the properties of one member of a series, would know what properties to expect in adjacent members. In re Henze, 85 USPQ 261 (1950), In re Wood, 199 USPQ 137 (CCPA 1978) and In re Lohr, 137 USPQ 548, 549 (CCPA 1963). The reasonable expectation of success derives from the fact that it is well established that the substitution of methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results. There would also be a reasonable expectation of success for the reason stated above (i.e., structurally similar compounds possess similar properties and, therefore, similar activities). As stated in the MPEP § 2144.08 (4. II A. (d)) "In re Grabiak, 769 F.2d 729, 731, 226 USPQ 870, 871 (Fed. Cir. 1985) ("When chemical compounds have very close structural similarities and similar utilities, without more a prima facie case may be made."). Thus, evidence of similar properties or evidence of any useful properties disclosed in the prior art that would be expected to be shared by the claimed invention weighs in favor of a conclusion that the claimed invention would have been obvious. Dillon, 919 F.2d at 697-98, 16 USPQ2d at 1905; In re Wilder, 563 F.2d 457, 461, 195 USPQ 426, 430 (CCPA 1977); In re Linter, 458 F.2d 1013, 1016, 173 USPQ 560, 562 (CCPA 1972)". Applicant also argues that when considered as a

whole, Castro *et al.* teaches away from the use of the morpholine substituent because compound 35 has a higher IC50 value than the compounds that do not have morpholine as a substituent. This argument is not found to be persuasive because even though the morpholine substituted compound 35 has a higher IC50 value than the non-morpholine substituted versions, it still does, in fact, inhibit IKK. Therefore, the fact that it inhibits IKK would provide enough motivation to one skilled in the art to make additional morpholine substituted compounds (i.e., one with a methyl substituent on the morpholine) and to test out their activity against IKK. In other words, the motivation would have been to make additional compounds which could possibly be used to inhibit IKK. For all the reasons stated above, the examiner has established a *prima facie* case of obviousness and the rejection is maintained.

Maintained Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 9 and 17 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over new claims 30-35 of copending Application No. 11/101,998. Although the conflicting claims are not identical, they are not patentably distinct from each other because conflicting claims 30-35 provide compounds and pharmaceutical compositions which overlap with applicants instantly claimed elected invention. For example, the instant claims 1 and 9 are drawn to compounds wherein A can be a morpholinyl ring substituted with multiple R6b groups and W-G wherein W can be Q- C=O. Therefore, it would have been obvious to one of ordinary skill in the art to make some of the compounds of the instant claims given copending Application No. 11/101,998. The motivation would have been to make additional compounds for the quoted purpose.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Maintained Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 9 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Castro et al. (C1 reference on 1449 and U reference on 892).

Determining the scope and contents of the prior art

Castro et al. discloses the compound 35 and registry no. 590398-98-4 useful to inhibit IKK for the treatment of certain inflammatory diseases (pages 2419 and 2421 and abstract).

Ascertaining the differences between the prior art and the claims at issue

The difference between the prior art and the claims at issue is that the prior art provides an unsubstituted ring A wherein ring A of the instant claims is substituted by at least one of C(R9)3, W-G or G, wherein C(R9)3 can be methyl. Therefore, the difference between the instant claims and the prior art can be a hydrogen versus a methyl on the morpholine ring.

Resolving the level or ordinary skill in the pertinent art

However, minus a showing of unobvious results, it would have been obvious to one of ordinary skill in the art at the time of the invention to prepare compounds of applicants instant elected invention when faced with the prior art of Castro et al., which discloses compound 35 and registry no. 590398-98-4 which are useful as inhibitors of IKK for the treatment of certain inflammatory diseases. It is well established that the substitution of methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results. In re Wood, 199 U.S.P.Q. 137 (C.C.P.A. 1978) and In re Lohr, 137 U.S.P.Q. 548, 549 (C.C.P.A. 1963). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (i.e., inhibitors of IKK).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KRISTIN BIANCHI whose telephone number is (571)270-5232. The examiner can normally be reached on Mon-Fri 7am-3:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kamal A Saeed/
Primary Examiner, Art Unit 1626

Kristin Bianchi
Examiner
Art Unit 1626

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